

mary lymphedema (clinical classification).

Diagnosis	Frequency ^{22,31,32,39} (% of all primary forms)
<i>Congenital (onset <2 years after birth)</i>	6-12
Familial, autosomal dominant (Nonne-Milroy disease)	
Familial, non-dominant inheritance	
Sporadic (most common congenital form)	
<i>Lymphedema precox (onset between 2-35 years)</i>	77-94
Familial, autosomal recessive (Meige disease)	
Sporadic (83-94% of all lymphedema precox)	
<i>Lymphedema tarda (onset after 35 years of age)</i>	11

Figure 1A

Functional Classification of Primary Lymphedema

	Distal Obliteration (80%)	Proximal Obliteration (10%)	Hyperplasia* (10%)
Gender	Female	Male or female	Male or female
Onset			
Time	Puberty	Any age	Congenital
Location	Ankle; bilateral	Whole leg, thigh; unilateral	Whole leg; unilateral or bilateral
Progression	Slow	Rapid	Progressive
Family history	Frequently positive	None	Frequently positive

Adapted from Browse NL: The diagnosis and management of primary lymphedema. *J Vasc Surg* 3:181, 1986.

*With or without reflux of chyle.

Figure 1B

Secondary lymphedema.

Blockade at the level of the lymph node
 Regional lymph node dissection
 Axillary (post-mastectomy lymphedema)
 Pelvic and para-aortic (leg and groin lymphedema)
 Neck (head and neck lymphedema)
Neoplastic disease
 Hodgkin lymphoma
 Metastatic cancer
 Prostate cancer
 Cervical cancer
 Breast cancer
 Melanoma

Disruption or obliteration of lymphatic channels
 Surgery, e.g. ilio-femoral bypass
 Direct injury, e.g. trauma of the medial aspect of the thigh
 Radiation-induced fibrosis
 Neoplastic infiltration of lymphatic channels
 Rheumatoid arthritis
 Filariasis
 Recurrent infection, e.g. erysipelas

Figure 1C

Lymphangiographic Patterns

Normal vs. Primary Lymphedema

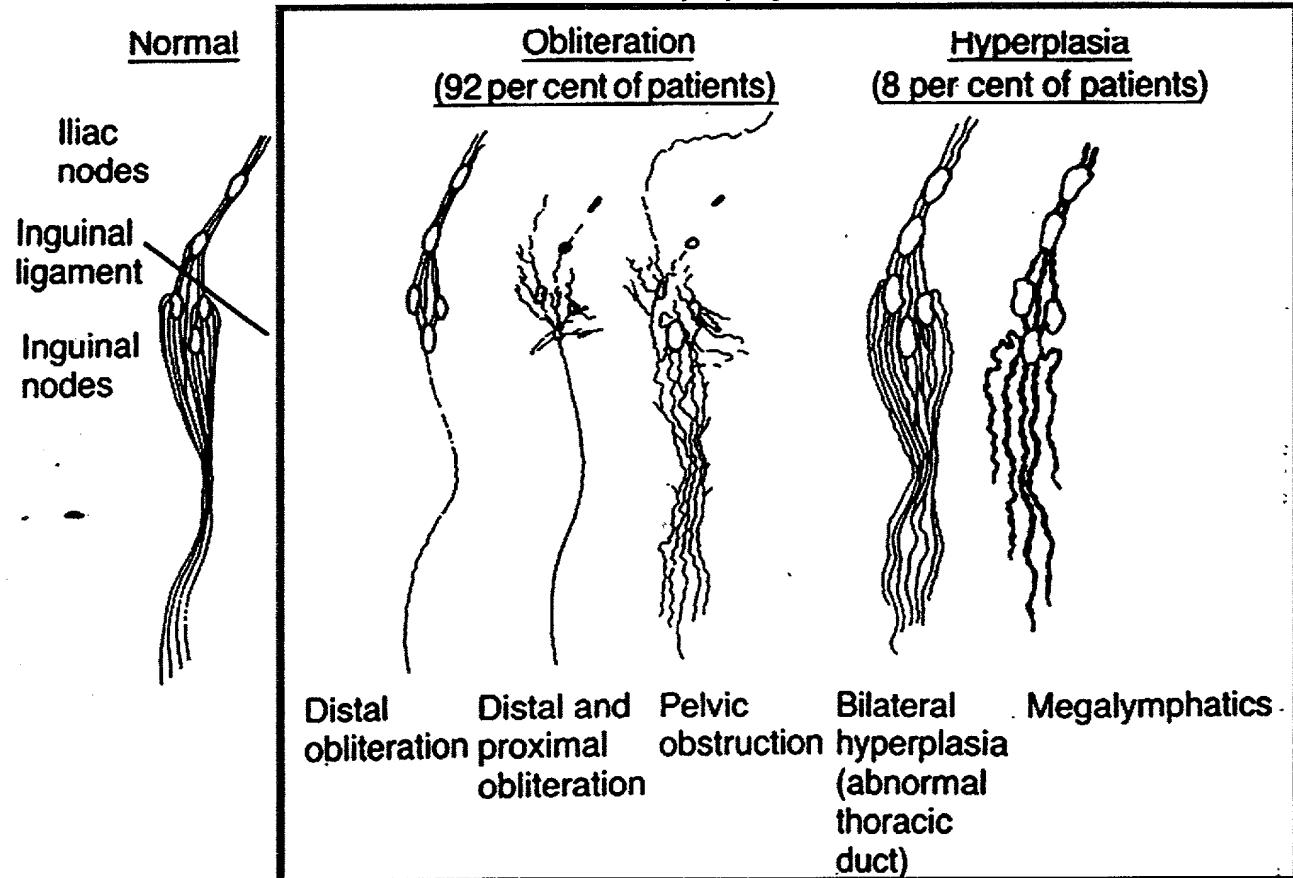


Figure 2

Rabbit Ear Lymphedema Model

Clinical Appearance - 5 Month



Control

VEGF-2

Figure 3

Rabbit Ear Lymphedema Model
Lymphoscintigraphy - 5 Month Post-Op

VEGF-2

*CONTROL

Figure 4

Rabbit Ear Lymphedema Model
Lymphoscintigraphy-Orientation

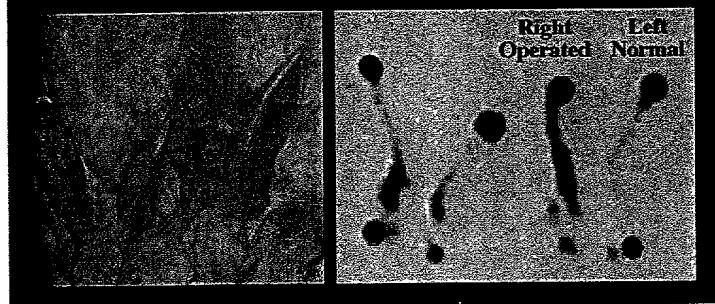


Figure 5

Rabbit Ear Lymphedema Model
Lymphoscintigraphy-Early Post-Op

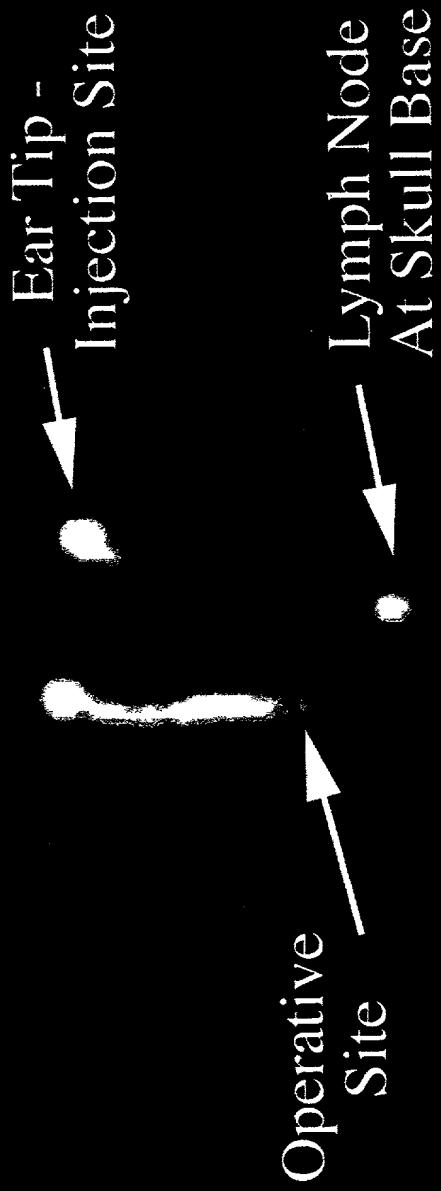


Figure 6

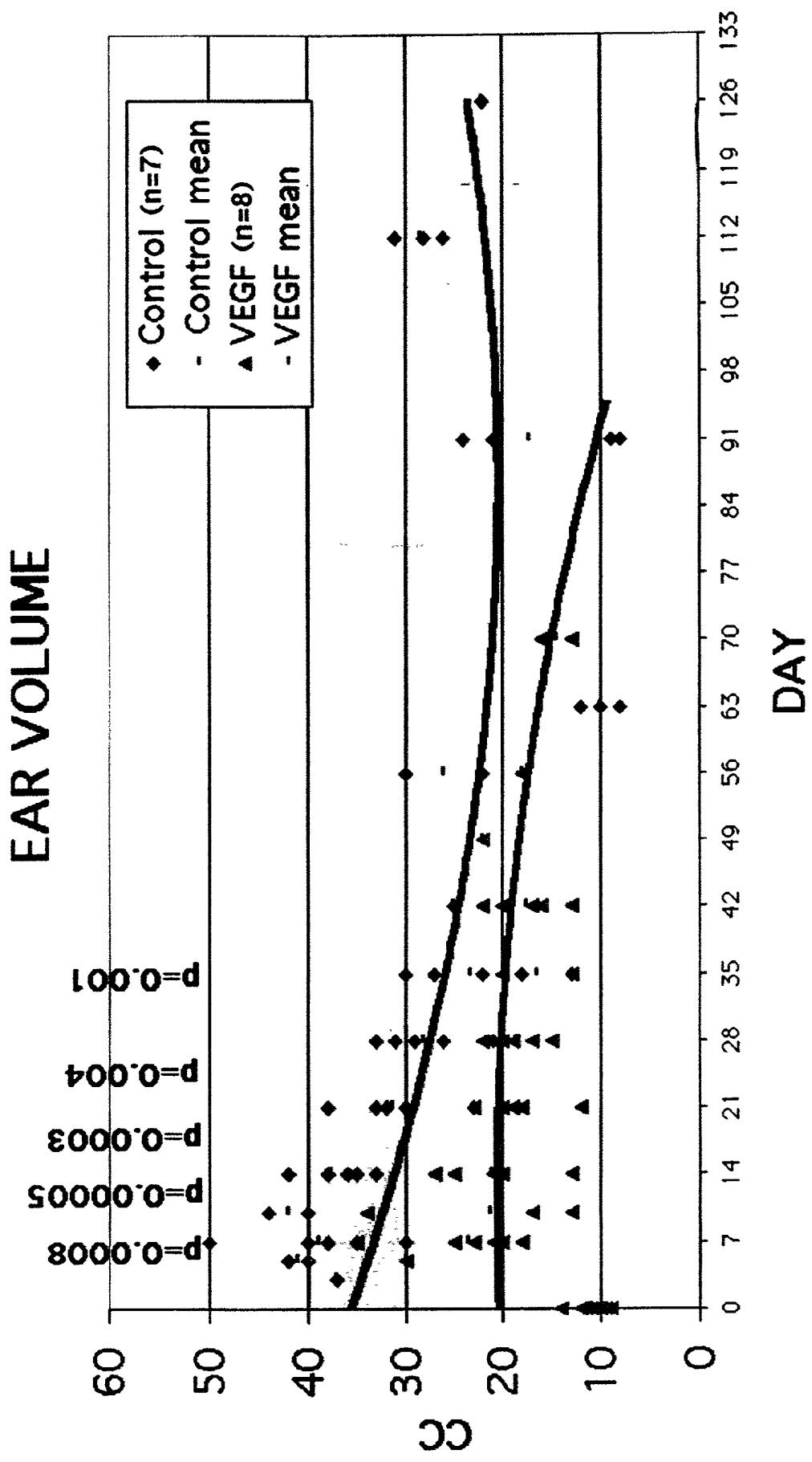


Figure 7

Rabbit Ear Lymphedema Model 3 Days Post-Op

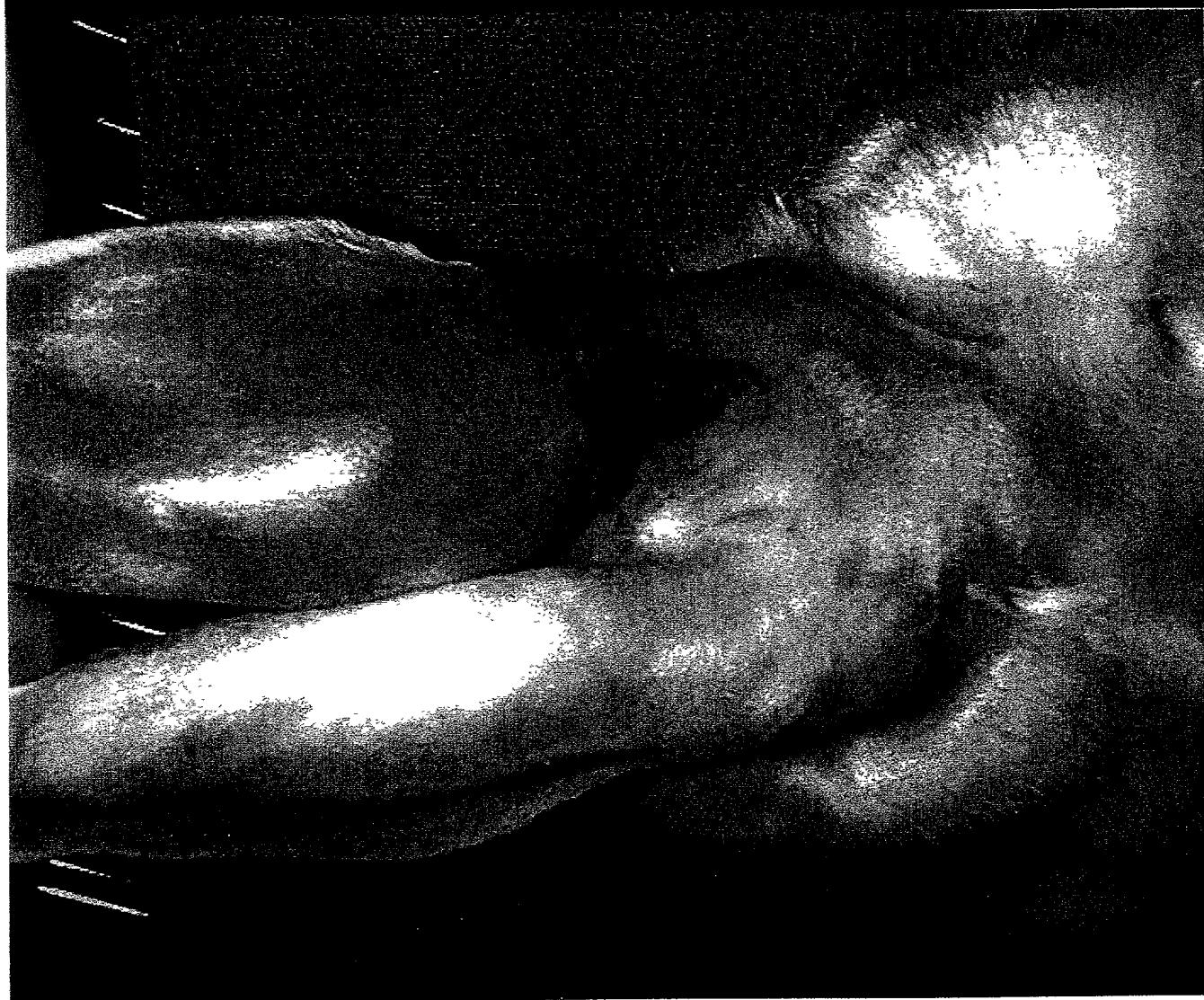


Figure 8

Human Lymphoscintigraphy Right Lower Extremity

Pre-VEGF2

Post-VEGF2

Thigh



Knee



Foot

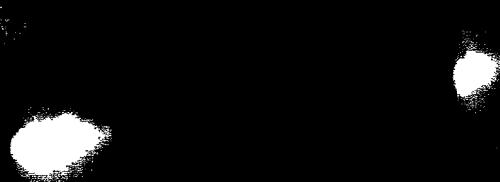


Figure 9

Ultrasound Imaging of Intra-Muscular VEGF-2 Gene Transfer: Lymphedema

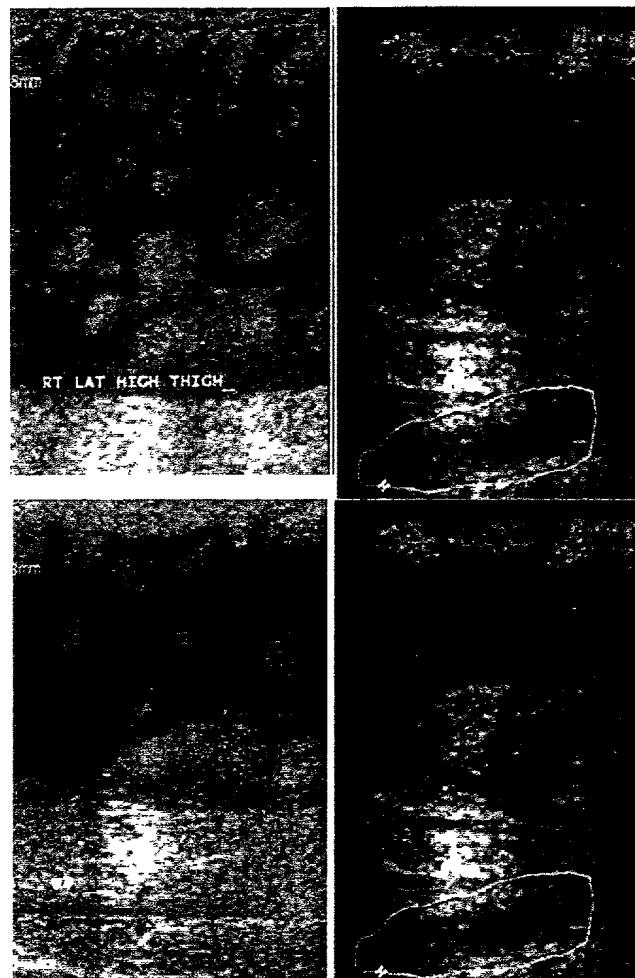


Figure 10

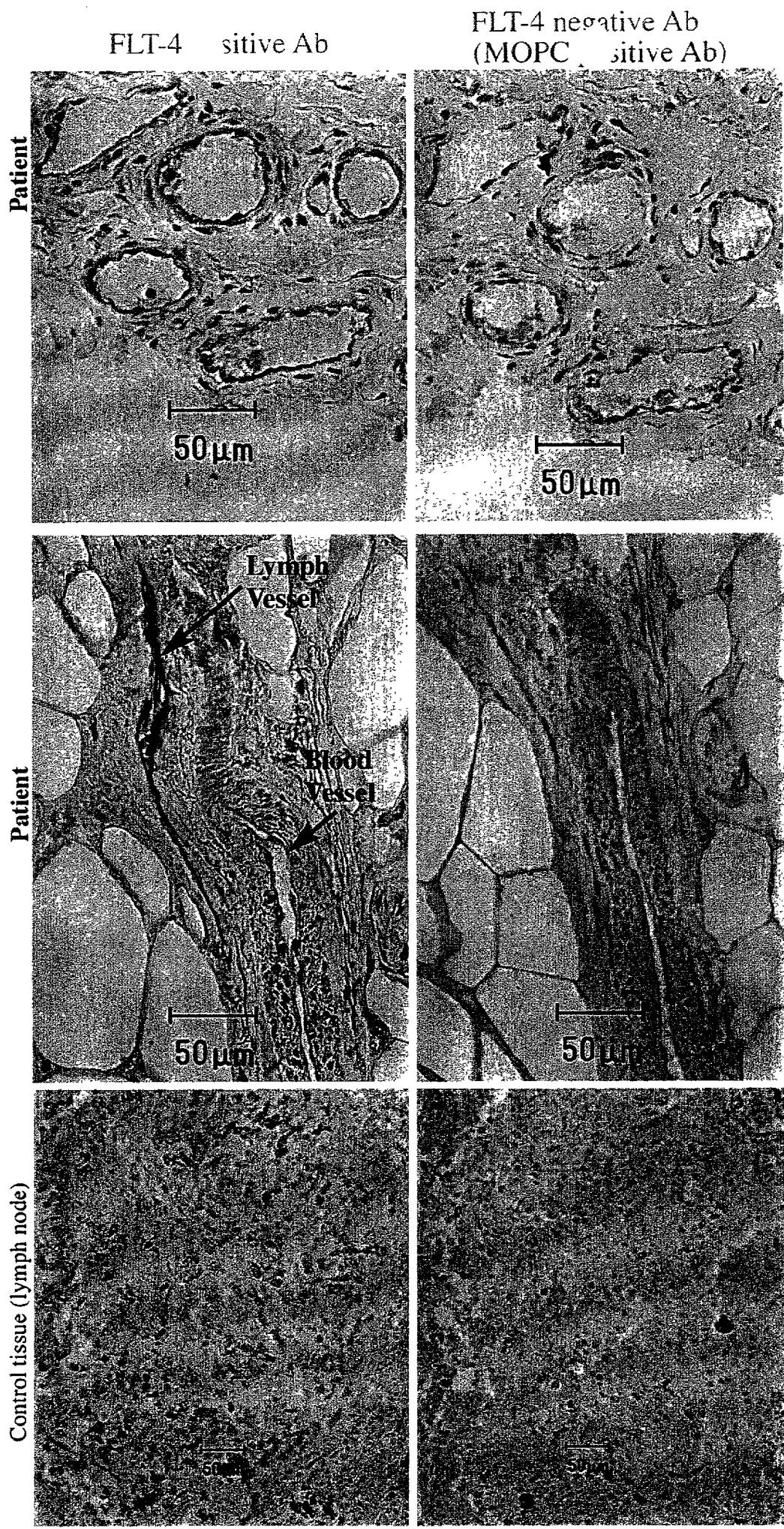




Fig. 12A



Fig. 12B

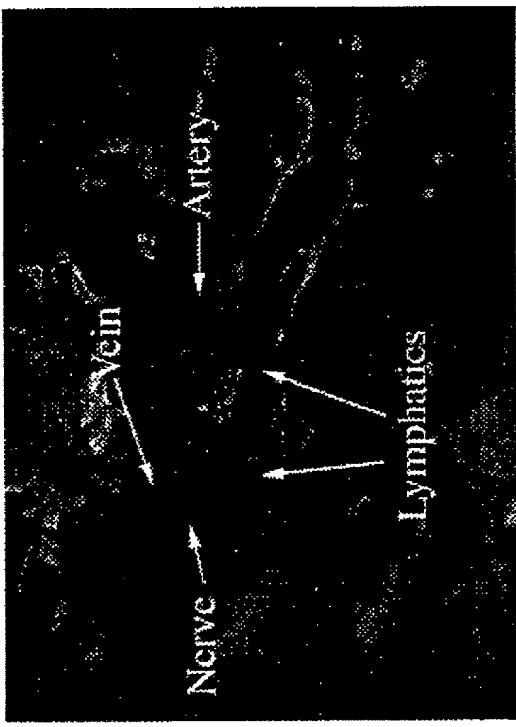


Fig. 12C

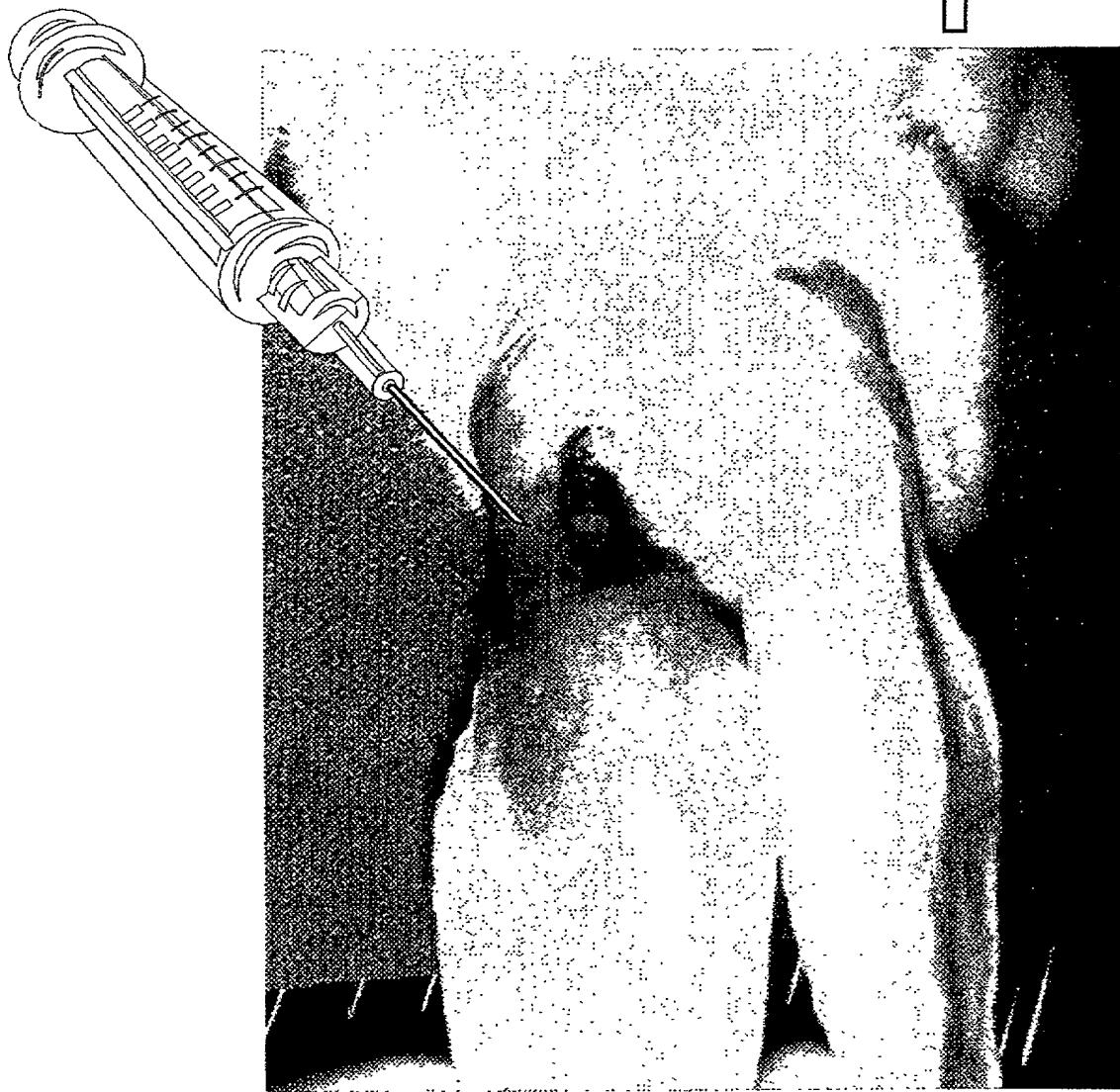
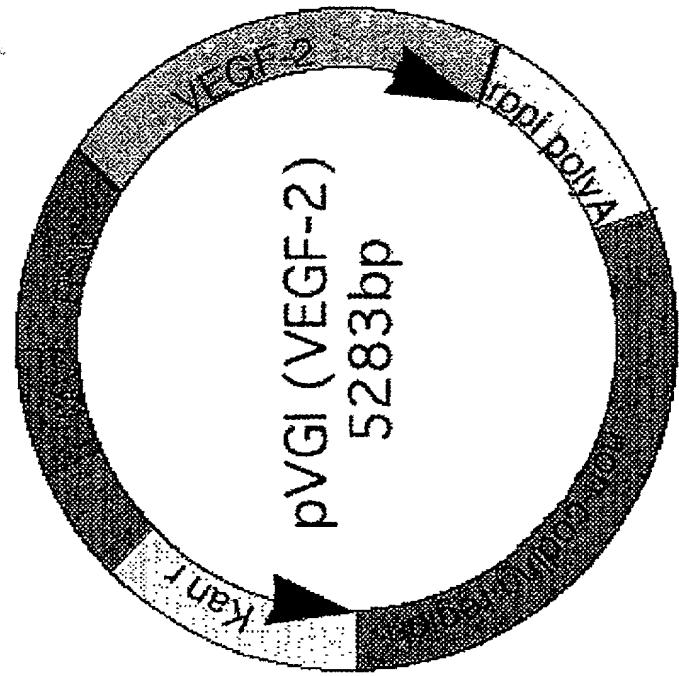


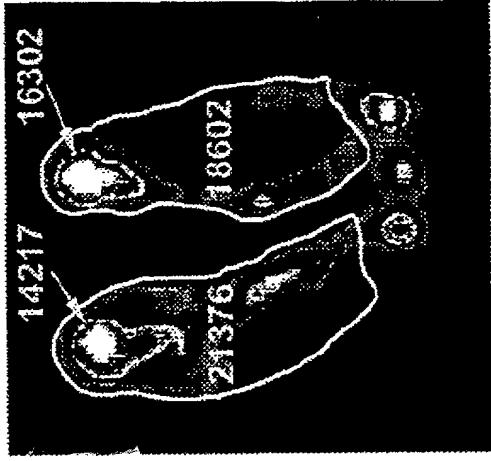
Fig. 13A

D1 D6 D11

Fig. 13B

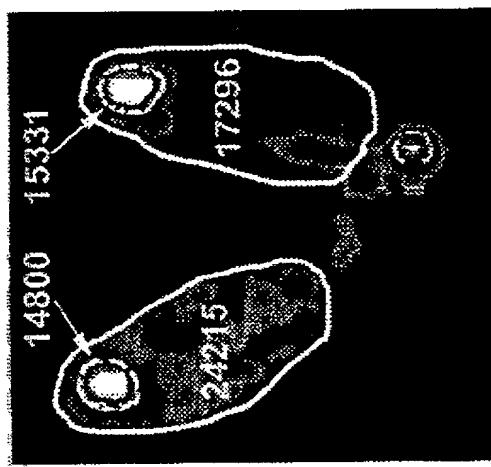


Figs. 14 A-C



$$\begin{aligned} & (24125-14800)/(17296-15331) \\ & = 4.75 \end{aligned}$$

Fig. 15A



$$\begin{aligned} & (21376-14217)/(18602-16302) \\ & = 3.11 \end{aligned}$$

Fig. 15B

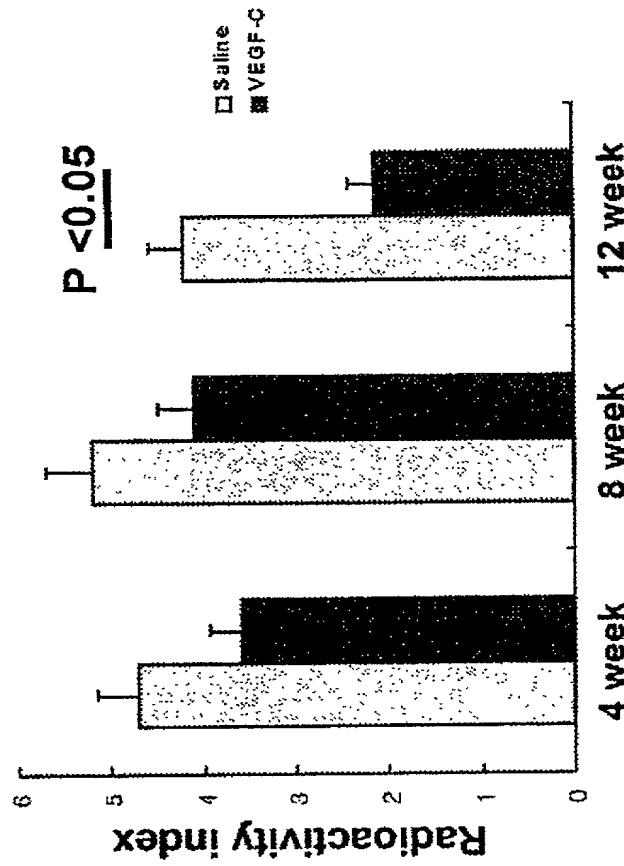


Fig. 15C

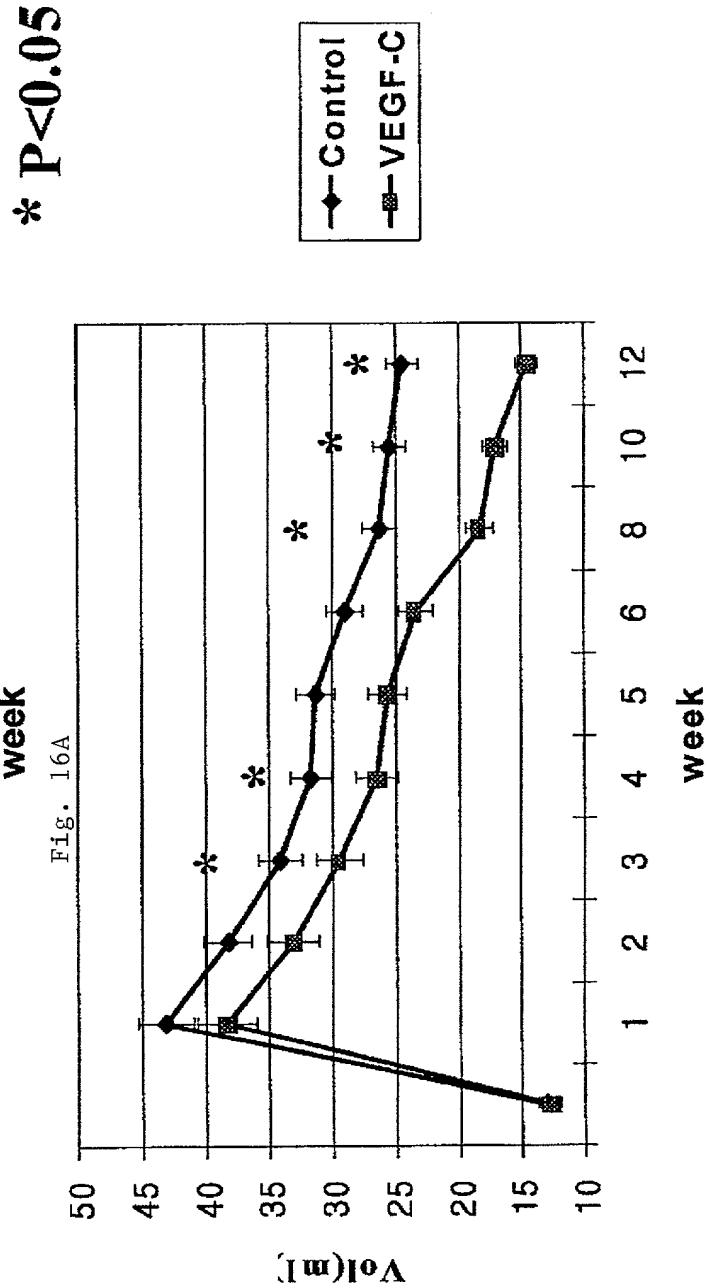
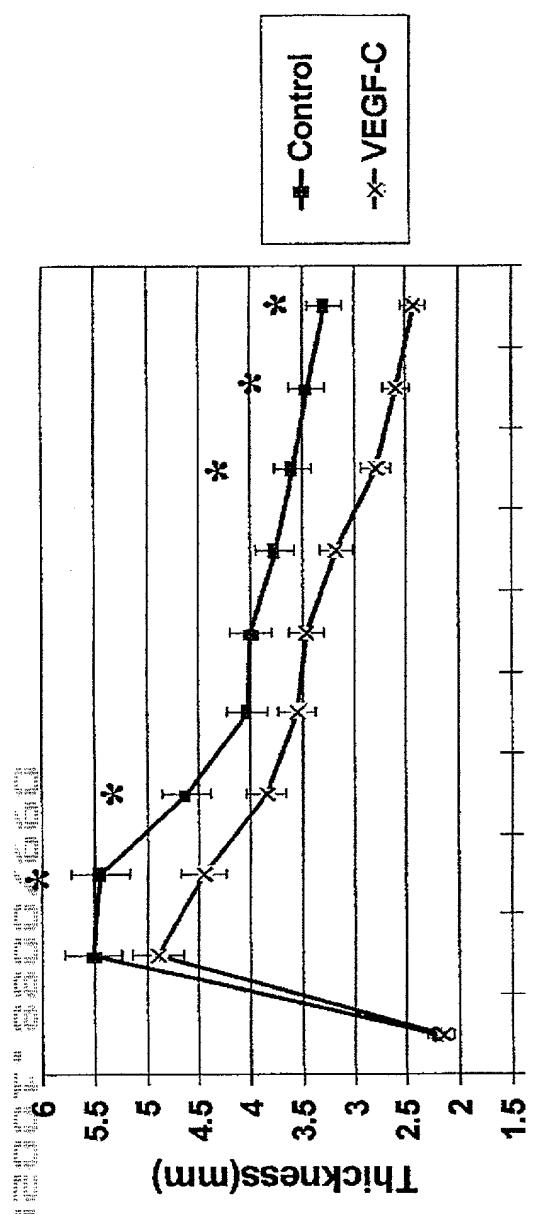
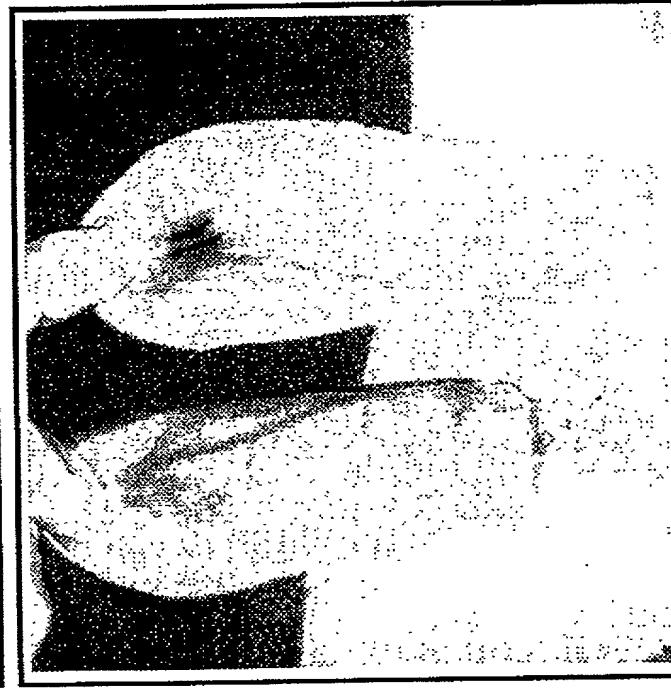
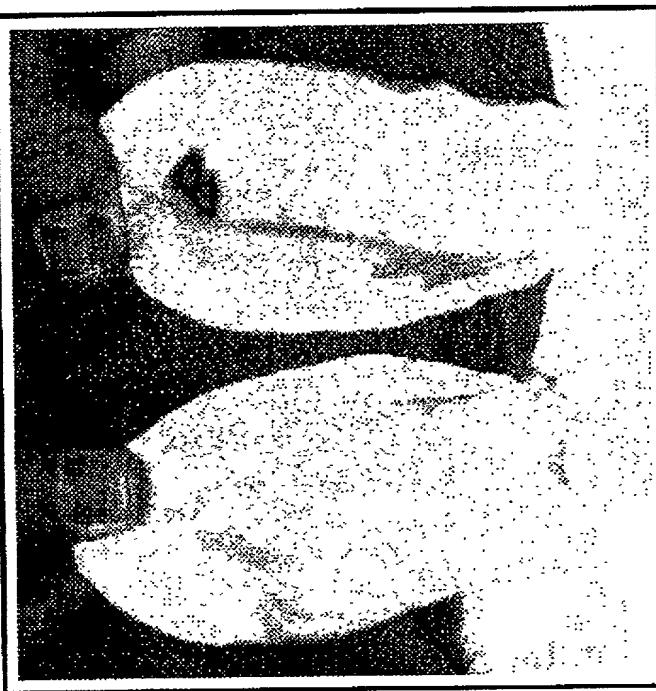


Fig. 16B

Fig. 16A

* P<0.05

Figs. 17 C-D



Control

VEGF-C

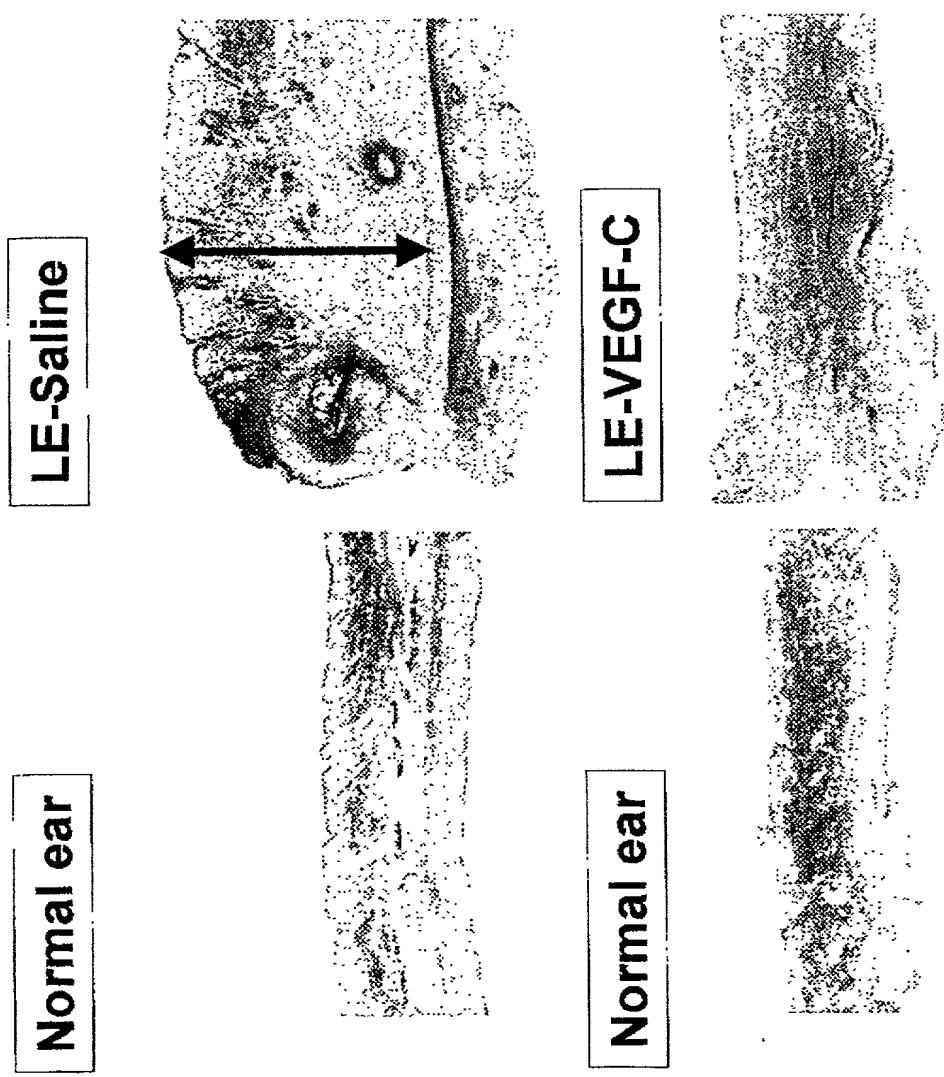


Fig. 18A

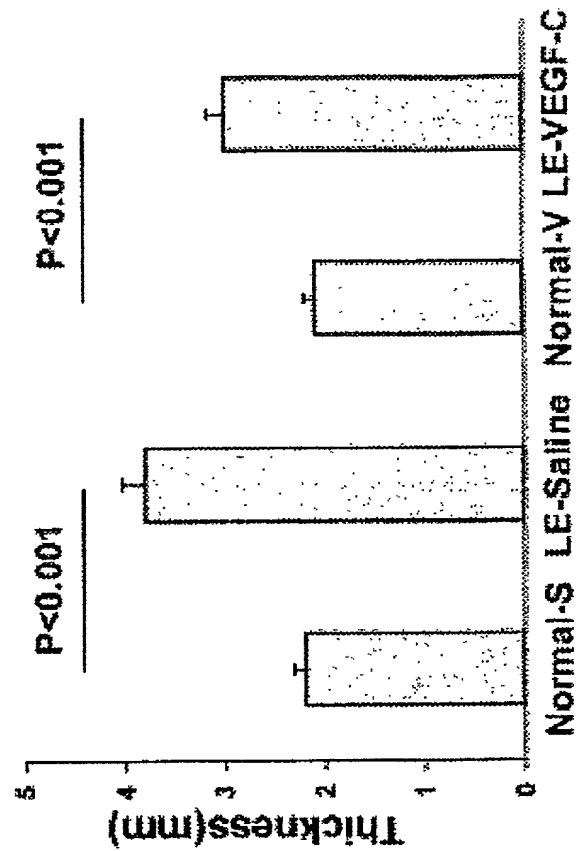
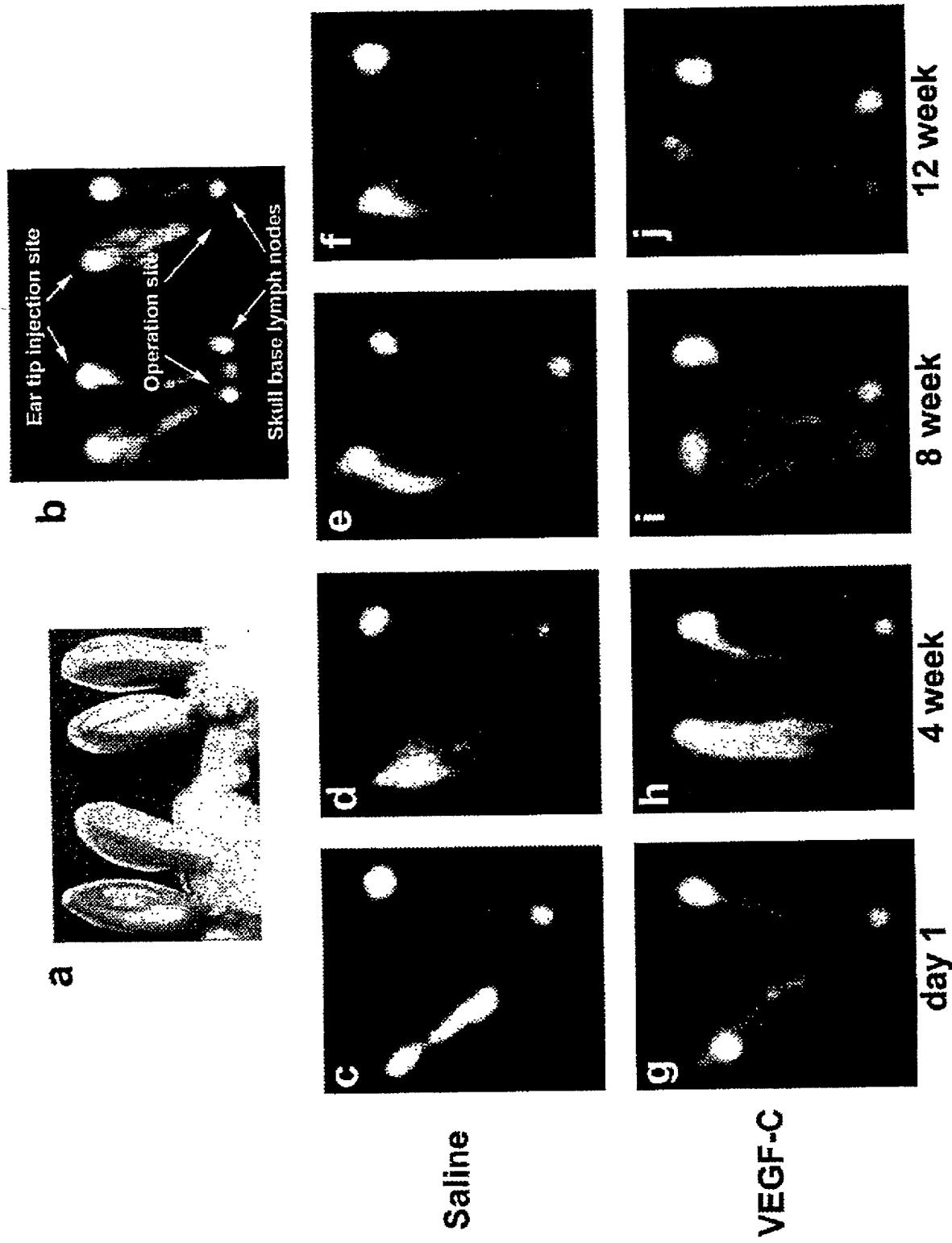


Fig. 18B



Figs. 19 A-J

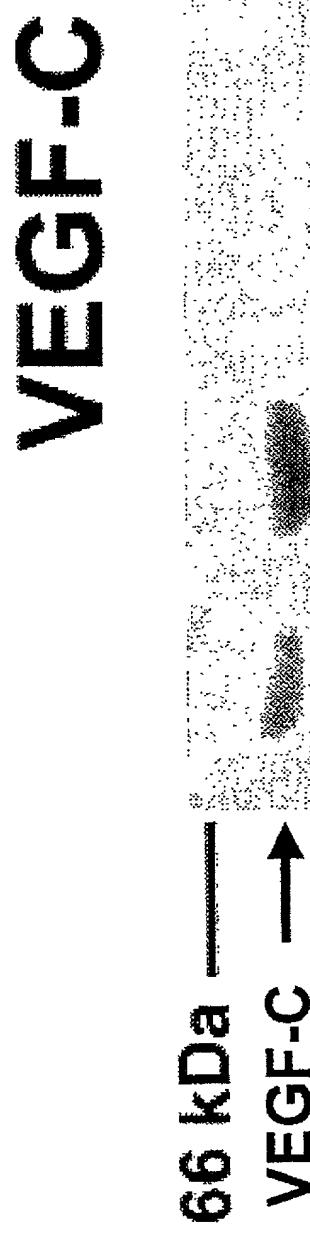


Fig. 20A

α -tubulin

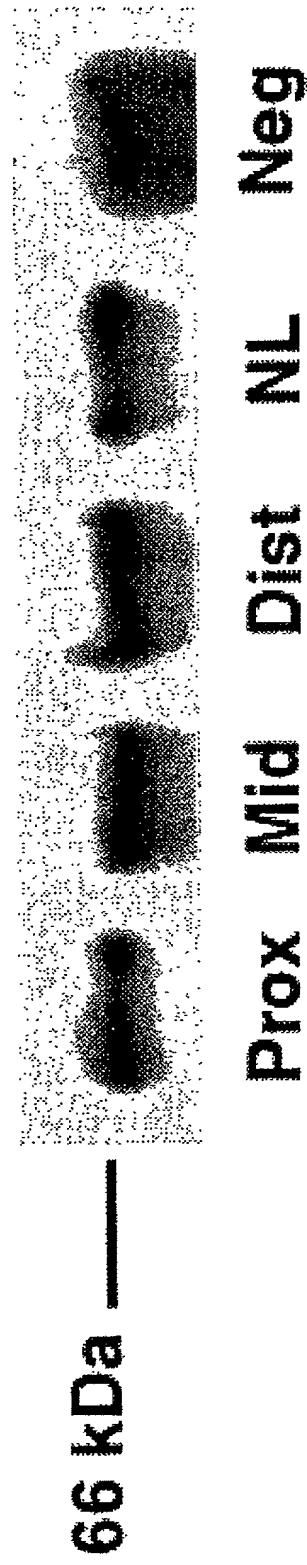


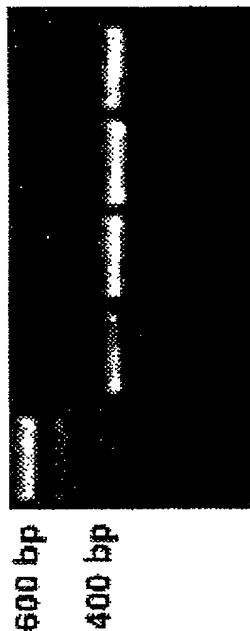
Fig. 20B

				1	CGGTGCGGA TGGCGGGGGC AGACGTGCC AGCATCGAT CGTACAAAGA
bo	1	CGGTGCGGA TGGCGGGGGC AGACGTGCC AGCATCGAT CGTACAAAGA			
hu	1	CGGTGCGGA TGGCGGGGGC AGACGTGCC AGCATCGAT CGTACAAAGA			
■o	1	CGGTGCGGA TGGCGGGGGC AGACGTGCC AGCATCGAT CGTACAAAGA			
rb	51	TCAGAGCTC CTGGAGAAC ATCTCGGAT CGACCTCGGG GACTCGGCC			
bo	51	TCAGAGCTC CTGGAGAAC ATCTCGGAT CGACCTCGGG GACTCGGCC			
hu	51	TCAGAGCTC CTGGAGAAC ATCTCGGAT CGACCTCGGG GACTCGGCC			
■o	51	TCAGAGCTC CTGGAGAAC ATCTCGGAT CGACCTCGGG GACTCGGCC			
rb	101	AGAGGGTGGAG CATCGAGGC GTGGCGGAGG AGGACCGGCG CGCTAATCTG			
bo	101	AGAGGGTGGAG CATCGAGGC GTGGCGGAGG AGGACCGGCG CGCTAATCTG			
hu	101	AGAGGGTGGAG CATCGAGGC GTGGCGGAGG AGGACCGGCG CGCTAATCTG			
■o	101	AGAGGGTGGAG CATCGAGGC GTGGCGGAGG AGGACCGGCG CGCTAATCTG			
rb	151	TGCAAGCTGTG ECAACGCAA GTCGCGCGTC AGCTCGCG AGCGCTGTC			
bo	151	TGCAAGCTGTG ECAACGCAA GTCGCGCGTC AGCTCGCG AGCGCTGTC			
hu	151	TGCAAGCTGTG ECAACGCAA GTCGCGCGTC AGCTCGCG AGCGCTGTC			
■o	151	TGCAAGCTGTG ECAACGCAA GTCGCGCGTC AGCTCGCG AGCGCTGTC			
rb	201	TGTGGAGGC CGCGAAGATA GAGGCGAGAT CGAGATCGT ATCGCTGG			
bo	201	TGTGGAGGC TGTAGGATA AAGGCGAGAT CGAGATCGT ATCGCTGG			
hu	201	TGTGGAGGC TGTAGGATA AAGGCGAGAT CGAGATCGT ATCGCTGG			
■o	201	TGTGGAGGC TGTAGGATA AAGGCGAGAT CGAGATCGT ATCGCTGG			
rb	251	GGACCGCGT CATCGCGCTT TCTCTGGG GCTCGATCTC GCTCGATCTC			
bo	251	GGACCGCGT CATCGCGCTT TCTCTGGG GCTCGATCTC GCTCGATCTC			
hu	251	GGACCGCGT CATCGCGCTT TCTCTGGG GCTCGATCTC GCTCGATCTC			
■o	251	GGACCGCGT CATCGCGCTT TCTCTGGG GCTCGATCTC GCTCGATCTC			
rb	301	TGTAACATCA CGACGCGAGC CGACGCGAGC ATCAAGACG GCTACCTTC			
bo	301	TGTAACATCA CGACGCGAGC CGACGCGAGC ATCAAGACG GCTACCTTC			
hu	301	TGTAACATCA CGACGCGAGC CGACGCGAGC ATCAAGACG GCTACCTTC			
■o	301	TGTAACATCA CGACGCGAGC CGACGCGAGC ATCAAGACG GCTACCTTC			
rb	351	CATCATCATG GATCGCGGG AGGTGCCTCT CGAGGAACAA TGTGATAACC			
bo	351	CATCATCATG GATCGCGGG AGGTGCCTCT CGAGGAACAA TGTGATAACC			
hu	351	CATCATCATG GATCGCGGG AGGTGCCTCT CGAGGAACAA TGTGATAACC			
■o	351	CATCATCATG GATCGCGGG AGGTGCCTCT CGAGGAACAA TGTGATAACC			
rb	401	TGTCTTACGA CGCGAGCGAG			
bo	401	TGTCTTACGA TGCAGTCKA			
hu	401	TGTCTTACGA TGCAGGCGAG			
■o	401	TGTCTTACGA CGCGAGCGAG			

Fig. 21

rb	1	RCAYAGAKHP	SIWIKDRL	LEEEGIDLA	DSNGPSLQR	YREEDAGRL
bo	1	RCPYAGATHP	SIWIKDRL	LEEEGIDLA	DSNGPSLQR	YREEDAGRL
hu	1	QCLYAGAKHP	SIWIKDRL	LEEEGIDLA	DSNGKLSQR	YREEDAGRL
■o	1	RCPYAGAKHP	SIWIKDRL	LEEEGIDLA	DSNGPSLQR	YREEDAGRL
rb	51	CSVNKAEGV	NSSASVAYGG	AEDRSSEMEIV	ILVGTGVAY	FFWVLLLLIF
bo	51	CSVNKAEGV	NSSASVAYEG	SEDKGSMEVY	ILVGTGVAY	FFWVLLLLIF
hu	51	CSVNKAEGV	NSSASVAYEG	SEDKGSMEVY	ILVGTGVAY	FFWVLLLLIF
■o	51	CSVNKAEGV	NSSASVAYEG	SEDKGSMEVY	ILVGTGVAY	FFWVLLLLIF
rb	101	DNWKPAAHD	IKIGYLSIM	DPGEPLEED	CEVLSYDASQ	
bo	101	DNWKPAAHD	IKIGYLSIM	DPGEPLEED	CEVLSYDASQ	
hu	101	DNWKPAAHD	IKIGYLSIM	DPGEPLEED	CEVLSYDASQ	
■o	101	DNWKPAAHD	IKIGYLSIM	DPGEPLEED	CEVLSYDASQ	

Fig. 22A



Mass Lung Kidney LA

Fig. 22B

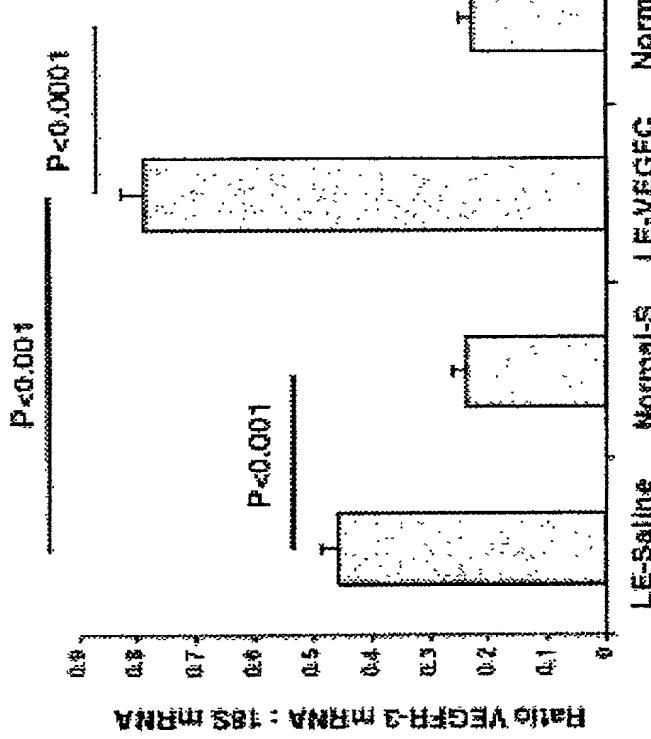
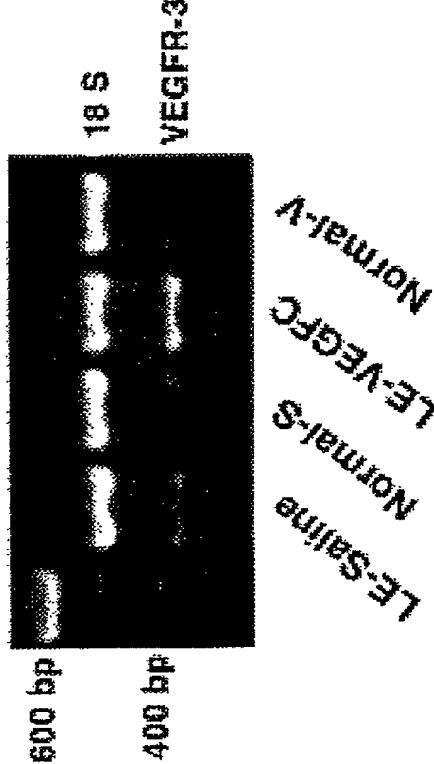


Fig. 22D



Mass Lung Kidney LA

Fig. 22C

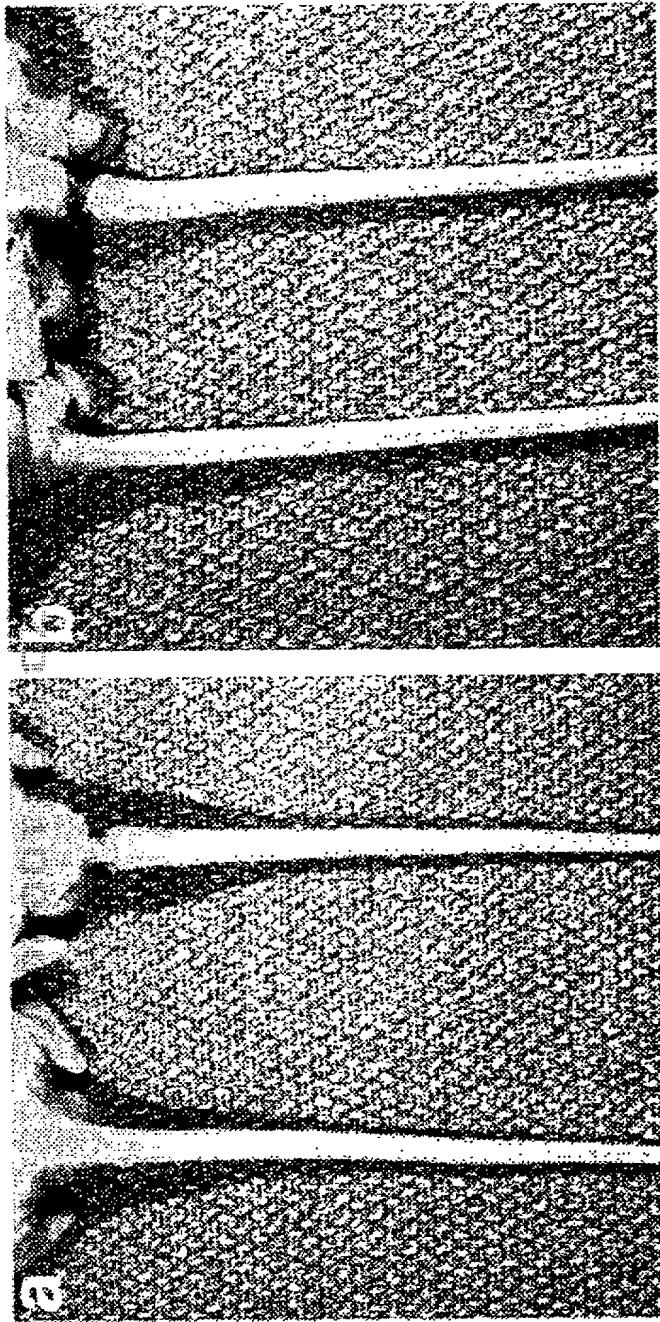


Fig. 23A

Fig. 23B

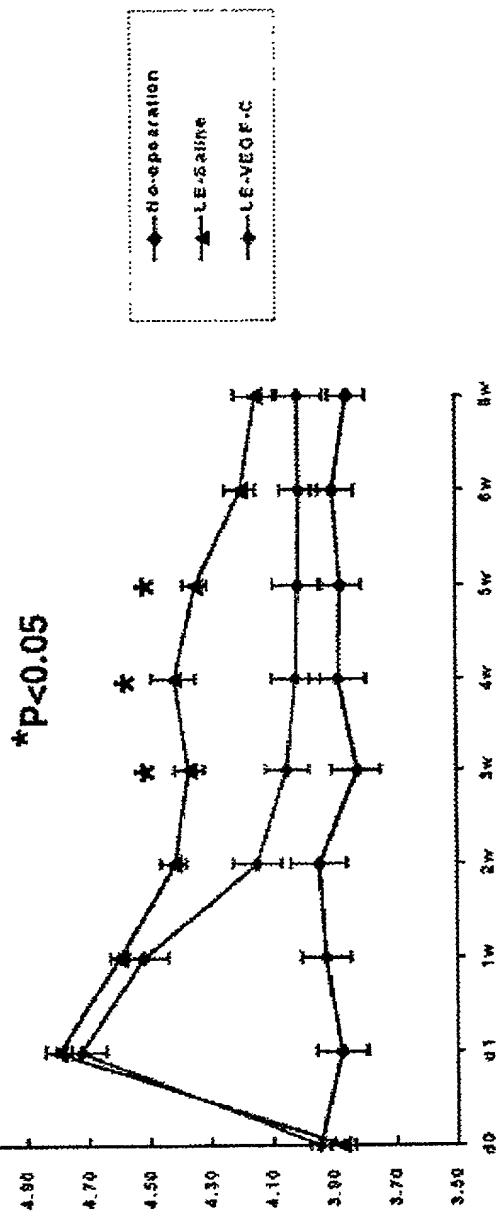
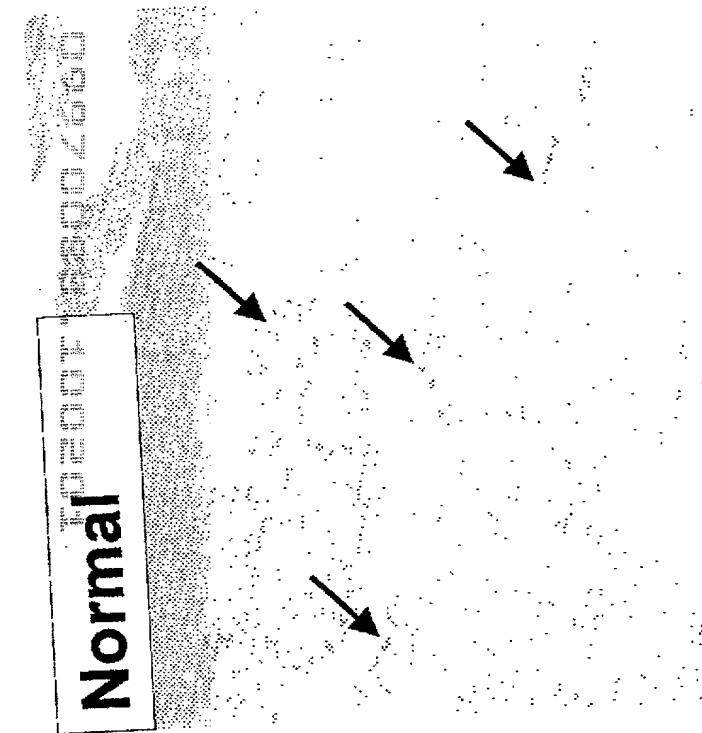


Fig. 23C

LE-Saline



Normal

Fig. 24 A-D

LE-VEGF-C

